



Newsletter for May 2023

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Strategies for Integument Modification

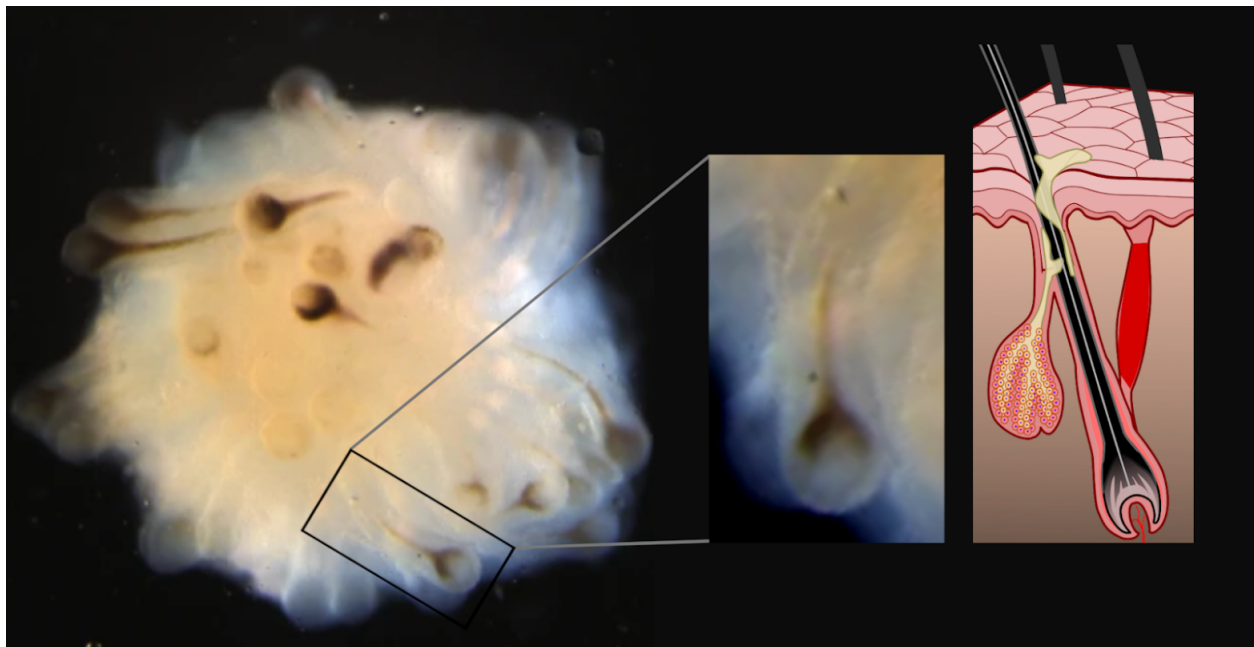
By Tilt Wolf | May 30, 2023

As the integument project wraps up its final report, we have uncovered some truly amazing advances in research that give us hope and confidence that our goals are close at paw! Over the course of the past ~2 years, we have done a deep dive into the literature

to understand what would be required, and what is left to do, to achieve stable introduction of fur, feathers, and scales into human skin.

For fur, we were thrilled to learn that last year in the lab of Dr. Karl Koehler at Harvard University, a method was discovered for producing competent human hair follicles *in vitro* that can be successfully transplanted into nude mice for growing mature hairs ([Lee et al., 2022](#)). It uses human induced pluripotent stem cells (iPSCs) treated with a series of factors including a TGF-beta inhibitor, recombinant BMP4, and recombinant bFGF in E8 Flex growth media (see the excerpted figure below, reproduced from Lee et al.). All things considered, it's a remarkably simple and elegant solution that solves a critical problem: the need to produce more follicles because humans do not have a sufficient number for fur coverage even when they are programmed to overgrow.

We have also identified essential pathways for controlling the characteristics of hair follicles, including width and length - we need knobs to turn so that coats of fur look realistic and



Hair follicle-bearing skin organoid grown *in vitro* by Lee et al. (2022), with a zoomed excerpt showing an individual transplantable follicle, and a cartoon (reproduced from WikiMedia) showing hair follicle anatomy for reference.

have species-appropriate features. FGF5 appears to be a strong candidate for hair length regulation, and Wnt10b is the clear candidate for width control, which we have focussed on as part of our first wet lab project - to develop a peptide inhibitor that interferes with Wnt10b to allow us to make follicles smaller or larger. We obtained recombinant Frizzled receptors, which are the proteins that cells use to recognize pro-growth signals from Wnt10b, and we are testing those against Wnt-derived peptides synthesized in a grid of peptides on a cellulose membrane. Although initial attempts resulted in technical issues from nonspecific background signal, we are circumventing the issue by using chemiluminescent detection instead to see whether peptides are interacting with the Frizzled receptors as we expect them to. If we identify specific peptide-receptor interactions, these peptides would serve as good candidates to turn the Wnt10b knob for controlling fur thickness - an important component, since nobody wants wiry human hair for fur!

For the next of the integument domains, feathers, we are proposing further experiments to attempt to reconstruct the feather development patterning mechanism in human cells. The patterning mechanism for feathers is known, with only one missing component that itself could be one of three possible proteins that are also known ([Li et al., 2017](#)). Our hope is that by adding avian versions, likely from the chicken genome, for all of the essential feather patterning genes along with structural genes they control, to human hair follicle cells, we will be able to reproduce feather-like development in mostly-human cells. Alternatively, if this strategy proves unsuccessful or otherwise is delayed, another possibility is to apply the hair follicle culturing methods to avian feather follicle cells and then xenotransplant them into human skin. However, this would also require co-transplantation of modified thymus cells to prevent immune rejection, because this type of artificially cultured

feather follicle would not be genetically human.

And for the final domain, we have designed a proposed solution for generating reptile-like scales on human skin, because the natural patterning mechanism for scales is not currently known. To recreate scales, we propose coupling tetracycline-inducible, optogenetic (light-sensitive), bistable gene switches to epidermis-thickening genes. These genes could include some combination of hard keratins and/or a subset of the genes involved in ichthyosis, a family of dermatological conditions that result in scaled, overly thickened skin. Our intention is to validate this hypothesis by adding the set of designed genes into epidermal germinal cells within cultured human skin, which can be conveniently obtained for experimentation as a live skin product called EpiDermFT, produced by MatTek Life Sciences.

We're genuinely excited for the conclusion of the project and all of the new project areas that will be born from it! Our final report is already over 100 pages, and we aim to publish it later this year. In the meantime, stay tuned this upcoming month for a more substantial project update containing excerpts of our proposed experiments.

Also, a big thank you to all of our volunteers that have worked on the project, including Lathreas, Rumi, and MacDaRacc currently, and formerly also Cam Cam, Atha, Birdy, and Rakeela. You are all awesome for making this happen!

Financial and compliance update

By Zennith | May 20, 2023

It's time for another financial and compliance update. For nonprofit organizations that have their financial year synchronized with the calendar year (which is most of them, including us), May 15th is the deadline for

submitting a Form 990 to the IRS, reporting on the prior year's financial results. Many states share the same deadline.

We submitted ours a bit early, actually, on March 12th! We've also been able to knock out several of the reports that we owe state authorities, and things look good on the fundraising registration compliance front.

Reduction in expenses and complexity

As compared to 2021, in 2022 we made some important changes to our organization that have helped our general and administrative expenses become more efficient.

First, we are no longer employing Keiro for part-time help with our Information Technology systems. Keiro is still with us as a board member and volunteer, and he's awesome! And Keiro was doing some incredible things for below-market rates. But, after carefully reviewing the sorts of infrastructure we needed, some things were looking like overkill (i.e., sufficient for organizations 10 times as large!), especially considering fairly low-maintenance commercial services.

Second, we were employing Atha part-time as well, for a mixture of compliance, outreach, and research work. Atha let us know in April of last year they intended to step down from their employed role for another opportunity. They were really kind and gave several months' notice of their intent; their last paid work for us was in late July 2022. Similar to Keiro, Atha was doing exemplary work in a cost effective way. However, after analyzing our needs, it once again looked like our investment was becoming overkill.

Compliance, especially, is getting dramatically easier than it was even 5 years ago. So many filings and reports have moved online. Also, the instructions provided by state governments for the sorts of forms, filings, and information they need have gotten substantially more clear and easy to take action on. Of course, there's also an element

of us understanding compliance better than a few years ago. We know the drill.

In 2019, it might have taken us at least 3-4 hours to file paperwork with a state by snail mail, and occasionally, paperwork even needed notarized! Notarization is...fine, but if you have several things that need notarized, and need physical/wet-ink signatures mailed across the country...it gets to be a lot. Now, depending on the state, it might be anywhere from 15 minutes to 1.5 hours to finish all of our obligations to the state for the year. That's a **big** difference.

Furthermore, there's a lot of overhead that comes with running payroll. Timesheets, paychecks, tax withholding, quarterly employment tax returns, and complex regulations meant we needed help from not one, but two accountants, since Keiro lives in the US and Atha lived in the UK during their employment. (We even had a UK entity, "Freedom of Form Foundation, Ltd", that brought its own paperwork). All of this was worth it - if things need to get done, they need to get done - but I don't miss the fees or the amount of work involved!

So, due to the above, we're looking at dramatically lower expenses, mainly for general and administrative functions. The reduction started to become visible in Q2 and really took off in Q3.

Prioritization in research purchases

In comparison, our research activities have been accelerating. Tiltwolf has been conducting wet-lab research to engineer the interaction between signaling proteins that can modify hair/fur growth. As well, Bleddyn, Nalco, and Mecknavorz have been purchasing tons of electronics for the Enhanced Tail project, working towards the goal of making tails that feel like they're part of you and behave naturally.

In short, we're spending money on actual experiments, in addition to our literature/background research. Both types of research

are needed to get something that works in real life. Without tangible experiments, of course, you can't get tangible results. And without carefully doing the literature/background research, you're just tinkering!

Financial summary

All of that puts us in a place where our results for 2022 make sense. Hint: they look very different from 2021!

As a disclaimer, we are using our best understanding of GAAP rules for the below, and we use cash basis accounting. However, our figures are not audited.

In 2022, we earned \$35,639.06 in revenues, spent \$24,493.30 in operating expenses, and recognize a loss equivalent presented as \$48.77 USD mostly due to reduction in the value of British Pounds held by our UK entity. These result in a net comprehensive income of \$11,096.99.

In terms of revenues, donors on Patreon led the way, generously giving us \$16,286.60. Next, we received \$10,552.46 from other sources, including a surprise \$10,000 donation from an anonymous donor via PayPal Giving Fund. Finally, donations from known major donors were \$8,800.00. Our major donors prioritize covering overhead expenses, and with lower overhead in 2022, we didn't need to phone in as many favors!

Expenses in several categories were smaller than 2021. We can slice the numbers at least two different ways, and we'll show both ways to give the full story.

Let's do the simpler way first - fairly close to the raw transactional data that the IRS checks for tax compliance. We spent \$3,323.13 on IT services and software; no large purchases of devices in the past year. \$1,986.38 went to organization taxes and licenses. We spent \$1,256.70 on legal and professional services,

Statement of cash flows

	2022	2021	2020	2019
Revenues				
Major donor donations	\$8,800.00	\$41,750.00	\$17,550.00	\$18,250.00
Donations through Patreon	\$16,286.60	\$12,482.60	\$8,968.53	\$5,129.95
Other donations	\$10,552.46	\$704.54	\$402.77	\$1,299.46
Terasem grant	-	\$1,000.00	-	-
Interest earned	\$0.00	\$0.09	-	-
Total revenues	\$35,639.06	\$55,937.41	\$26,921.30	\$24,679.41
Expenses				
Office supplies	-\$3,323.13	-\$5,484.46	-\$6,329.44	-\$2,610.33
Corporate taxes and licenses	-\$1,986.38	-\$966.99	-\$253.50	-\$195.00
Legal and professional services	-\$1,256.70	-\$21,344.05	-\$10,919.08	-\$8,210.42
Banking fees	-\$333.51	-\$703.06	-\$335.08	-\$278.83
Marketing	-\$641.29	-\$676.99	-\$593.34	-\$784.09
PRGM SVC - Purchases for research	-\$3,104.57	-\$201.61	-	-
PRGM SVC - Purchases for education and outreach	-\$1,026.08	-\$1,861.10	-\$2,328.36	-\$3,562.83
PRGM SVC - Academic grant	-\$2,550.00	-\$4,000.00	-	-\$4,000.00
Employee compensation	-\$9,924.22	-\$17,705.31	-\$4,568.16	-\$1,105.46
Payroll and employment taxes	-\$347.43	-\$1,265.89	-\$1,452.16	-\$314.12
Total expenses	-\$24,493.30	-\$54,209.46	-\$26,779.12	-\$21,061.08
Other revenues and expenses				
Currency fluctuations	-\$48.77	\$0.18	-	-
Total other revenues and expenses	-\$48.77	\$0.18	\$0.00	\$0.00
Net comprehensive income	\$11,096.99	\$1,727.95	\$142.18	\$3,618.33

Cash basis. Not audited.

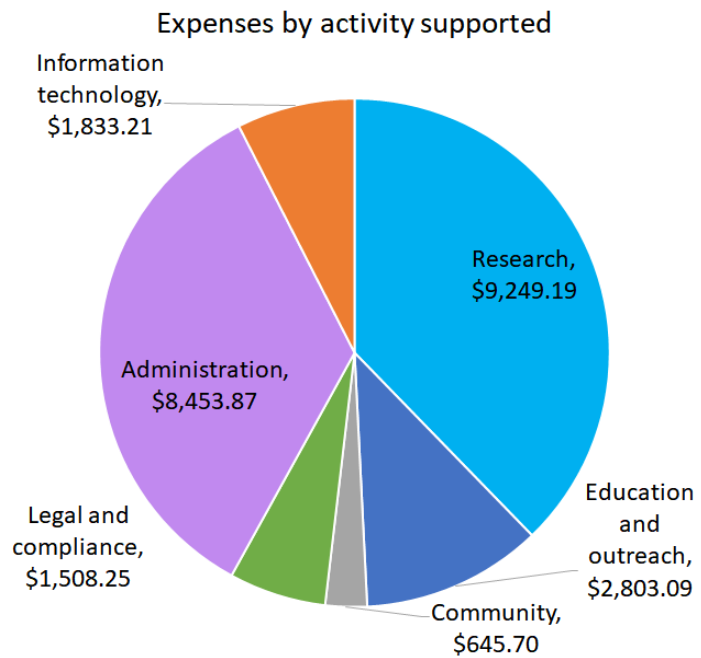
mainly accountants helping with payroll. \$333.51 went to banking and transaction fees, and \$641.29 for marketing. \$3,104.57 was used to purchase research supplies, most of which went to buying reagents for Tiltwolf's wet-lab research project. \$1,026.08 went to education and outreach activities, including getting one of our scientists who wouldn't have otherwise attended to join us at Anthro New England 2022 (Our appearance at Midwest FurFest 2022 was all on personal dollars). We used \$2,550.00 to defray open-access license costs for a journal article we had previously supported - while we don't exactly love that fee, ensuring open access to research is important to us. Finally, we spent \$9,924.22 on employee compensation as well as \$347.43 related payroll and employment taxes.

You can compare the above figures to previous years using the table on the previous page ("Statement of cash flows"). We've come a long way from prior years, that's for sure!

The other way of slicing the data follows how organizations use accounting to analyze results and make decisions, rolling employee-related expenses into the type of activity being supported. So, if the employee was doing compliance, IT, or research-related work, the corresponding fraction of expense would be attributed to that activity. Since we have kept track of how expenses including paid time were used, we can get an accurate bird's-eye view of the whole forest.

Going by this, we spent \$9,249.19 on research, \$2,803.09 on outreach, and \$645.70 on community functions, leading to a total spend on program services of \$12,697.98.

Overhead (general and administrative expenses) came to \$11,795.32, composed of \$1,508.25 on compliance/licenses/etc, \$8,453.87 in administration, and \$1,833.21 on IT.



Over half of our spend in 2022 was on program services, which is better than 2021 and 2020. While major donors continue to cover our overhead expenses - i.e., any donations you make aren't being used for all the administrative rigmarole - efficiency lets our resources go further than before.

We still have room to improve, but we're getting there. 2023 is on track to cut our overhead expenses in half again.

[You can view our filing with the IRS on our website here.](#) If you have any questions, please don't hesitate to reach out.

Thank you as always! Whether you're just stopping by, part of our community, a donor, or a volunteer, we appreciate you being a part of making the world a better place. Thank you!